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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	18

DATE MAILED: 1-13-97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 12/2/96 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1, 6-10, 12, 14, 16-28 are pending in the application.
   Of the above, claims 6-10, 12, 14, 16-20 are withdrawn from consideration.
2. ☒ Claims 2-5, 11, 13, 15 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1, 21-28 are rejected.
5. ☐ Claims _____ are objected to.
6. ☒ Claims 1, 6-10, 12, 14, 16-28 are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

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EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

Part III: Detailed Office Action

Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on 12/2/96 has been entered.

Claims 1 and 21-28 are under consideration.

The rejection of claims 1 and 21-26 under 35 U.S.C. §112, second paragraph, is withdrawn in view of applicants' amendments.

Formal Matters:

The disclosure is objected to because of the following informalities:

The brief description figure 9, as amended, does not correlate to the figure itself, as it is not clear what to what in the figure the description refers. Correction is required.

Double Patenting Rejections:

1, 21-30 Claims 1 and 21-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of U.S. Patent No. 5,010,010 for reasons of record in paper number 15, mailed 5/28/96, at page 5.

Applicants intention to overcome this rejection by submission of a terminal disclaimer is noted.

Objections and Rejections under 35 U.S.C. §112:

Claims 27 and 28 remain rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 27, the metes and bounds of "fully active in an adenylate cyclase

assay" are not clear; while a protein is described in the specification as being "fully active in an adenylate cyclase assay", the specification does not give any indication of what "full activity" is. Therefore, the metes and bounds of claims 27 and 28 are not clear.

Applicants argument that "It is the obligation of the Patent Office to provide some evidence or scientific reason to support its assertion" of indefiniteness, and that the term in question would be understood by those of ordinary skill in the art has been fully considered but is not deemed persuasive. The issue here is not one of scientific evidence, but rather of indefiniteness. It remains that "full activity" is a relative term, and would depend upon the specific assay used, the conditions under which it were performed, and to what the sample was being compared. Therefore, the term remains indefinite, as none of these parameters have been specified.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention

was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1 and 21-28 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Brewer et al., U.S. Patent Number 3,886,132 for reasons cited in the Office Action, paper number 8 mailed 9/8/95, at page(s)5-7.

At page 5 of the amendment filed 12/2/96 applicants argue that the Patent Office position presumes that during the isolation process of Brewer, neither sequencing errors nor *in situ* modification of the protein could have occurred, and that the only possible source of errors in the N-terminal sequence of the *synthetic* peptide would be post isolation errors. This argument has been fully considered but is not deemed persuasive. First, applicants admit that the Examiner's position (as set forth by applicants) is logical, but unsupported. However, applicants, while admitting the logic of the position have proffered no evidence or argument to shift the burden back to the Patent Office. A logical interpretation is all that is required to establish a *prima facie* case of anticipation or obviousness, and applicants have done nothing to overcome such, including suggesting any interpretation that would be more likely to be correct. Second, once again, applicants are erroneously concentrating on the *synthetic* peptide of Brewer, whereas the rejection is clearly over the *naturally occurring*, isolated hPTH of Brewer. The source of difference between the synthetic peptide and that disclosed by applicants is moot. As clearly stated in the previous Office Action, "Applicants argument that Brewer contains three incorrect amino acids in the disclosed sequence of the first 34 amino acids of the protein is not persuasive, both because the claims contain no limitation as to particular sequence, and because, even if Brewer sequenced the protein incorrectly, the protein itself, which was obtained from the natural

source, appears to meet the limitations of the claims." Applicants have not argued this point.

Applicants argument that Brewer's peptide was not recombinantly produced has been fully considered but is not deemed persuasive. As stated in the original rejection, mailed 9/8/95:

> The decisional law has clearly emphasized that such claims are directed to a product and are not restrictive to a process because they are not construed as being limited to the product of a specific process (*In re Bridgeford*, 149 USPQ 55: *In re Hirao*, 190 USPQ 15). Patentability depends on whether the product is known in the art or obvious, and is not governed by its process of production (*In re Klug*, 142 USPQ 161); therefore, the burden is upon applicants to establish a patentable difference between the claimed product and that of the prior art (*In re Fessman*, 180 USPQ 324). Further held was that when a prior art product reasonably appears to be the same as that claimed, but differs by the process via which it was produced, a rejection of this nature is eminently fair and the burden is upon applicants to prove, by comparative evidence, a patentable difference (*In re Brown*, 173 USPQ 685; *In re Marosi*, 218 USPQ 289; *In re Thorpe*, 227 USPQ 965; *In re Fitzgerald*, 205 USPQ 594; and as more recently emphasized in *Ex parte Gray*, 10 USPQ 2d 1922; *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 9 USPQ 2d 1833; and *Scripps Clinic v. Genentech Inc.*, 3 USPQ 2d 1481). In view of the fact that the courts have clearly emphasized that product-by-process (p-b-p) claims are not patentable over product claims unless there has been established a patentable difference, one having ordinary skill in the art at the time of the invention would have expected that the hPTH produced by organic synthesis or by the recombinant process disclosed in the instant specification would be functionally/biologically equivalent to native hPTH as purified by Brewer et al. and would therefore function in a manner taught by the prior art, thus rendering applicant's claims prima facie obvious in the event that the claim is not anticipated by the prior art.

At pages 5-6 of the amendment, applicants argue that the protein of Brewer et al. cannot have been pure enough to meet the limitations of the claims, in view of the previous arguments of the Kimura, Fairwell, and Kumagaye references. This argument has been fully considered but is not deemed persuasive. The Kimura, Fairwell, and Kumagaye references are not analogous to Brewer, as they relate to purification of synthetic hPTH, as opposed to Brewer's isolation of naturally occurring hormone. The ordinary artisan would immediately recognize that the nature of the impurities in a natural preparation would be substantively different from those obtained

in an *in vitro* peptide synthesis. Whereas an *in vitro* synthesis would yield an initially heterogeneous mix of a variety of closely related products (having terminated at different steps of the synthesis of being differentially derivatized), one would not expect such a mix of closely related species in a preparation obtained from the natural source. It is further noted that Figure 2 of Kimura, to which applicants refer, is an HPLC chromatogram of the crude product obtained from peptide synthesis, and has no bearing on the naturally occurring product.

The Examiner does not find applicants continuing arguments that the protein of Brewer cannot meet the purity limitations of the claims, as the metes and bounds of "essentially pure" have not been set forth clearly in the specification. It remains that, in the absence of any evidence which would establish that recombinantly produced protein is patentably superior in purity to that purified by Brewer, that the claimed proteins remain anticipated or obvious over Brewer. In further support of this position, the Examiner takes note of the language of, for example, claim 21, which specifically recites "wherein said hPTH possesses biological activity *equivalent* to naturally occurring hPTH." If, as applicants now allege, recombinantly produced hPTH were of a purity superior to the naturally occurring protein, the biological activity of such, which is generally measured in terms of activity per unit of protein, would be ***higher than***, as opposed to equivalent to that of protein purified from the natural source.

Advisory Information:

No claim is allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.129(a) and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.129(a). Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the submission under 37 CFR 1.129(a). See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 8:00 A.M. to 4:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Stephen Walsh, can be reached at (703)308-2957.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The Art Unit 1812 Fax Center number is (703) 308-0294. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the Examiner at the telephone number above when a fax is being transmitted.

Informal communications only may be submitted by E-mail to Lorraine.Spector@exchange.uspto.gov. No amendments or formal communications may be sent via E-mail.

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Stephen Walsh
STEPHEN WALSH
SUPERVISORY PATENT EXAMINER
GROUP 1800